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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,324	08/23/2001	Tully Michael Underhill	3477.92	6862

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EXAMINER
DI NOLA BARON, LILIANA

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/856,324	Applicant(s) UNDERHILL ET AL.	
	Examiner Liliana Di Nola-Baron	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *16,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17-21 and 24-26* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-15, 17-21 and 24-26 in Paper No. 9 is acknowledged.

2. Applicant's amendment and arguments with respect to claims 16, 22 and 23, filed on December 16, 2002, have been considered, but they are not persuasive, since the methods of Groups II, III and IV, which are claimed in claims 16, 22 and 23 respectively, are not related to the invention of Group I, which is directed to a composition and methods of treatment or for promoting chondrogenesis comprising said composition. Accordingly, the restriction requirement is made final. Claims 1-15, 17-21 and 24-26 will be examined in this Office action. Claims 16, 22 and 23 are withdrawn from consideration.

Priority

3. Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) is acknowledged. However, the patent upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 2-4, 6 and 8 of this application.

4. Regarding claims 2-4, the foreign patent is silent with respect to generic or specific osteogenic proteins, cytokine and combinations thereof.

5. Regarding claim 6, the patent discloses a pharmaceutical composition by means of a biodegradable sponge, gel or paste (See p. 7, lines 26-28), but there is no mention in the patent of composition in the form of pill, tablet or encapsulated within liposomes.

6. Regarding claim 8, the patent does not disclose a biodegradable implantable matrix. The biodegradable sponge encompassed by the patent does not provide support for a matrix.

7. For the reasons above, foreign priority will not be considered for the subject matter claimed in claims 2-4, 6 and 8, and the effective priority date for said claims is the international filing date, November 19, 1999.

Information Disclosure Statement

8. The information disclosure statement filed on February 15, 2002 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office. It has been placed in the application file, and the information referred to therein has been considered, however, Applicant is required to submit a list of the information submitted for consideration by the Office.

Specification

9. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

10. Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Claim 18 should depend on claim 17 and not on subsequent claim 19.

Claim Rejections - 35 USC § 112 and 35 USC § 101

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 9-11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims read on the use of a composition, without specifying the method involved and the steps contemplated in the method of use.

Claims 9-11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1-15, 17-21and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/08546.

The patent provides pharmaceutical compositions comprising an RAR antagonist and a pharmaceutically acceptable carrier and methods comprising administering said compositions for the treatment of physical disorders, including rheumatoid arthritis (See p. 10, lines 6-27). The patent teaches that the compositions may be administered in several ways, including orally and parenterally, specifically by intraarticular injection (See p. 20, lines 13-25), and contemplates matrices of the drug in biodegradable polymers for injectable forms, and capsules, tablets, pills, powders and granules for oral administration (See p. 21, line 18-30). The patent teaches that the solid dosage forms may comprise coatings for differential release (See p. 22, lines 14-19) and the compositions may be administered in the form of liposomes (See p. 24, lines 4-12). The patent contemplates administration of the compositions in vitro, ex vivo or in vivo to cells (See p. 24, lines 14-22).

Thus, the patent provides pharmaceutical compositions comprising an RAR antagonist and a carrier and methods of treatment comprising administering said compositions, as claimed in the instant application. The patent is deficient in the fact that it does not specifically mention additional osteogenic factors, such as BMP, OPS, bone or collagen in the compositions of the invention, however, it contemplates administering said compositions in combination or coincidental with other drugs (See p. 24, line 27 to p. 25, line 11), thus, one of ordinary skill in

the art would have combined the RAR antagonist with additional osteogenic factors to obtain a more efficacious treatment.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of the patent to device pharmaceutical compositions and methods of treatment comprising administering said compositions, and include in said compositions additional drugs or osteogenic factors for the development of bones. The expected result would have been a successful pharmaceutical composition and successful methods of treatment. Because of the teachings of the patent, that the compositions of the invention can be administered, in vitro, ex vivo or in vivo in various forms and may be used for the treatment of arthritis, one of ordinary skill in the art would have a reasonable expectation that the compositions and methods claimed in the instant application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

16. Claims 1-15, 17-21and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Basset et al. (U.S. Patent 6,184,256).

The patent provides pharmaceutical compositions comprising an RAR antagonist and a pharmaceutically acceptable carrier and methods comprising administering said compositions for the treatment of physical disorders, including arthritis and osteoporosis (See col. 8, line 16 to col. 9, line 19). The patent teaches that the compositions may be administered in several ways,

including orally and parenterally, specifically by intraarticular injection (See col. 20, lines 11-37), and contemplates matrices of the drug in biodegradable polymers for injectable forms and capsules, tablets, pills, powders and granules for oral administration (See col. 21, lines 9-42). The patent teaches that the solid dosage forms may comprise coatings for differential release (See col. 21, lines 47-59) and the compositions may be administered in the form of liposomes (See col. 22, lines 57-59). The patent contemplates administration of the compositions in vitro, ex vivo or in vivo to cells (See col. 23, lines 6-19).

Thus, the patent provides pharmaceutical compositions comprising an RAR antagonist and a carrier and methods of treatment comprising administering said compositions, as claimed in the instant application. The patent is deficient in the fact that it does not specifically mention additional osteogenic factors, such as BMP, OPS, bone or collagen in the compositions of the invention, however, it contemplates administering said compositions in combination or coincidental with other drugs (See col. 23, lines 32-40), thus, one of ordinary skill in the art would have combined the RAR antagonist with additional osteogenic factors to obtain a more efficacious treatment.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of the patent to device pharmaceutical compositions and methods of treatment,comprising administering said compositions, and include in said compositions additional drugs or osteogenic factors for the development of bones. The expected result would have been a successful pharmaceutical composition and successful methods of treatment. Because of the teachings of the patent, that the compositions of the invention can be

administered, in vitro, ex vivo or in vivo in various forms and may be used for the treatment of arthritis, one of ordinary skill in the art would have a reasonable expectation that the compositions and methods claimed in the instant application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

17. Claims 2-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bollag et al. (U.S. Patent 6,326,397).

The patent provides compositions comprising retinoid antagonists and a carrier for the treatment of patients suffering from osteoporosis or arthritis, and teaches that retinoid antagonists increase bone formation, which is a function of osteoblasts that build up the matrix comprising type I collagen and proteins (See col. 7, line 17 to col. 9, line 49). The patent contemplates combining the retinoid antagonists with other active substances into one pharmaceutical composition and teaches that the compositions may be administered orally, in the form of tablets, pills or granules (See col. 11, lines 17-63).

Thus, the patent provides pharmaceutical compositions comprising an RAR antagonist and a carrier and methods of treatment comprising administering said compositions, as claimed in the instant application. The patent is deficient in the fact that it does not specifically mention additional osteogenic factors, such as BMP, OPS, bone or collagen in the compositions of the invention, however, it contemplates administering said compositions in combination with other drugs (See col. 11, lines 17-26), and teaches that bone formation depends on osteoblasts that build up the matrix comprising type I collagen and proteins, thus, one of ordinary skill in the art

would have combined the RAR antagonist with additional osteogenic factors, specifically type I collagen and osteogenic proteins, to obtain a more efficacious treatment.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of the patent to device pharmaceutical compositions and include in said compositions additional drugs or osteogenic factors for the development of bones. The expected result would have been a successful pharmaceutical composition. Because of the teachings of the patent, that the compositions of the invention are effective in the treatment of arthritis and osteoporosis, one of ordinary skill in the art would have a reasonable expectation that the compositions claimed in the instant application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

2&h03

February 20, 2003

James M. Spear

JAMES M. SPEAR
PRIMARY EXAMINER
AU 1615